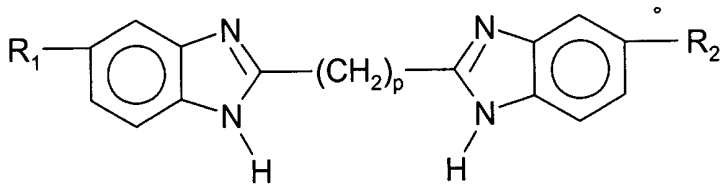
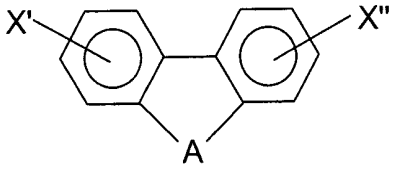
A 2

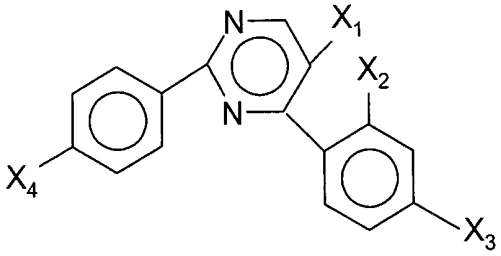
1. (once amended) A method of treating infection bursal disease (IBD) in an avian subject in need of such treatment, said method comprising administering to said subject a compound selected from the group consisting of:



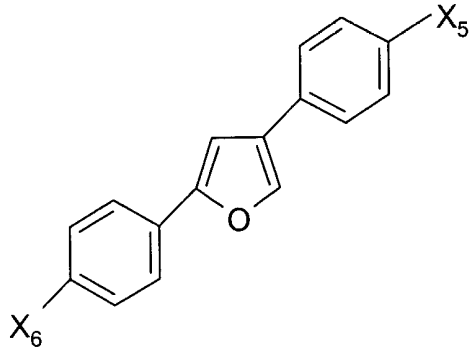
(I)



(II)



(III)



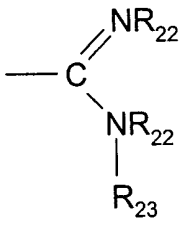
(IV)

or the pharmaceutically acceptable salts thereof, wherein :

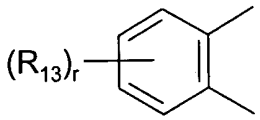
p is an integer ranging from 1 to 8;

A is selected from O, S, and NR wherein R may be H or loweralkyl;

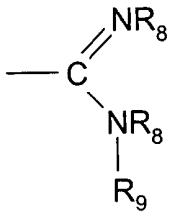
X', X", X_3, X_4, X_5, X_6, R_1, and R_2 are independently selected and each represented by loweralkyl, loweralkoxy, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, alkylaryl, halogen, or:



wherein each R_{22} and R_{23} is independently selected from the group consisting of H, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, and alkylaryl, or two R_{22} groups together represent C_2-C_{10} alkyl, hydroxyalkyl, or alkylene; or the two R_{22} groups together represent cycloalkyl or:



wherein r is from 1 to 3 and R_{13} is H,



or $-CONHR_{10}NR_{11}R_{12}$, wherein:

A1 cont

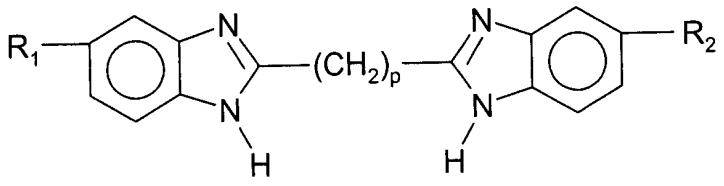
R_{10} is loweralkyl; R_{11} and R_{12} are independently selected from the group consisting of H and lower alkyl; each R_8 is independently selected from the group consisting of H, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, and alkylaryl, or two R_8 groups together represent C_2-C_{10} alkylene; R_9 is H, hydroxy, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, or alkylaryl; wherein X' and X" may be in the meta or para positions;

X_1 and X_2 are independently selected from H, loweralkyl, or loweralkoxy;

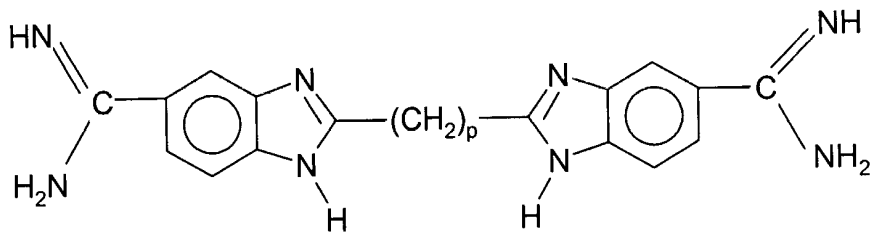
and wherein said compound thereof is administered in an amount sufficient to treat IBD.

A2

3. (once amended) The method according to Claim 1, wherein said compound is represented by the formula:

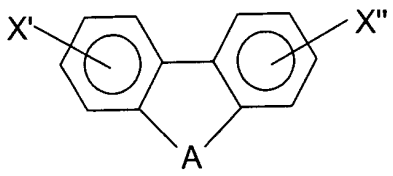


4. (once amended) The method according to Claim 1, wherein said compound is represented by the formula:

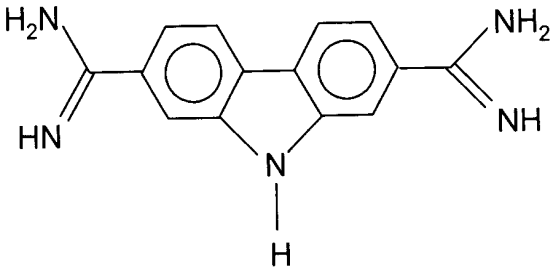


A2 Cont

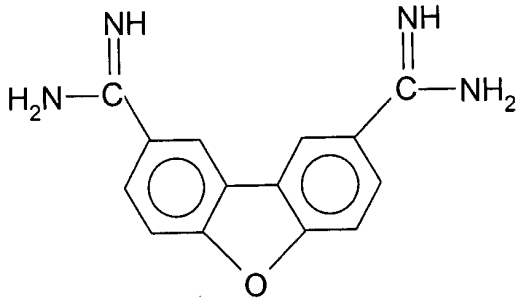
5. (once amended) The method according to Claim 1, wherein said compound is represented by the formula:



6. (once amended) The method according to Claim 5, wherein said compound is represented by the formula:

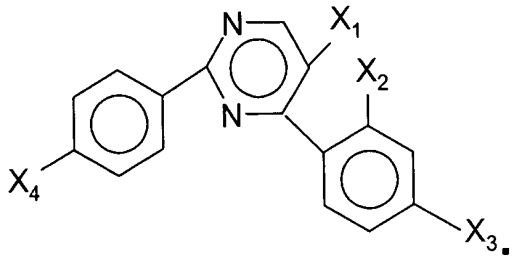


7. (once amended) The method according to Claim 5, wherein said compound is represented by the formula:

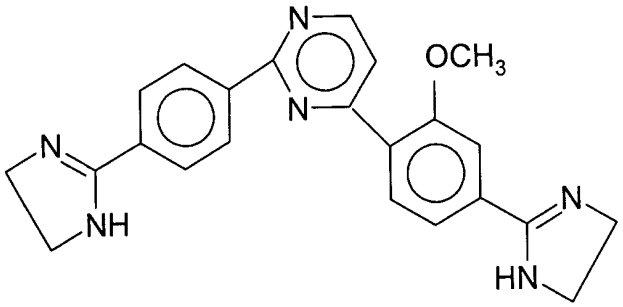


A2 cont

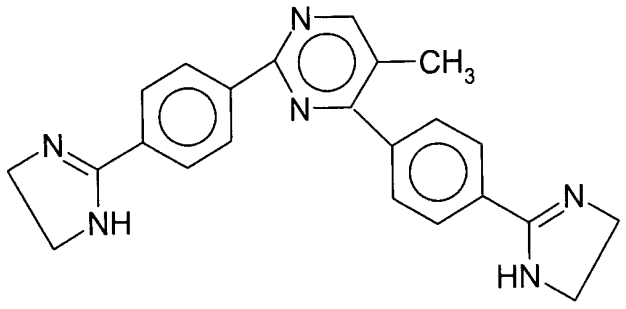
8. (once amended) The method according to Claim 1, wherein said compound is represented by the formula:



9. (once amended) The method according to Claim 8, wherein said compound is represented by the formula:

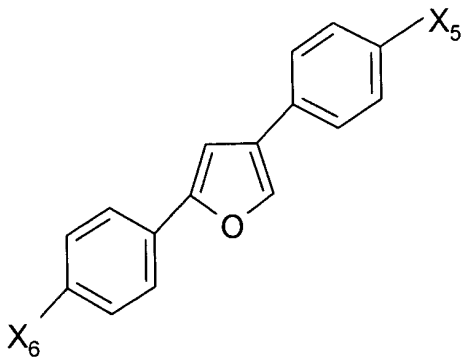


10. (once amended) The method according to Claim 1, wherein said compound is represented by the formula:

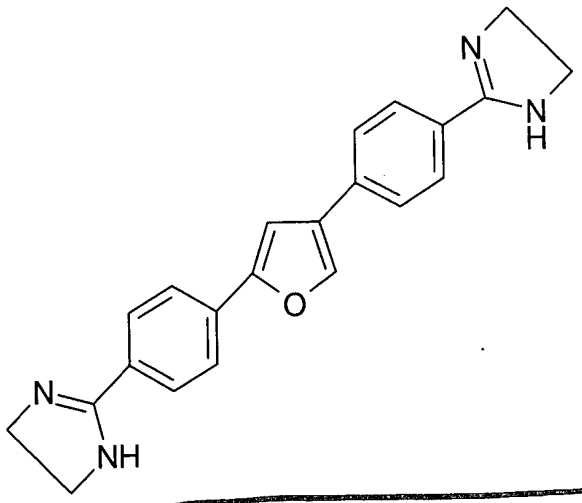


A2 cont

11. (once amended) The method according to Claim 1, wherein said compound is represented by the formula:

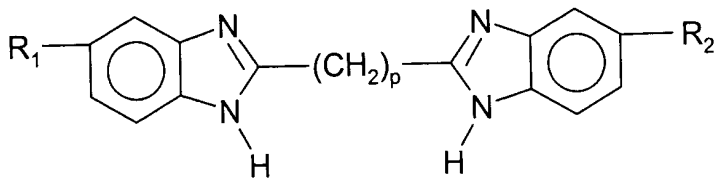


12. (once amended) The method according to Claim 1, wherein said compound is represented by the formula:

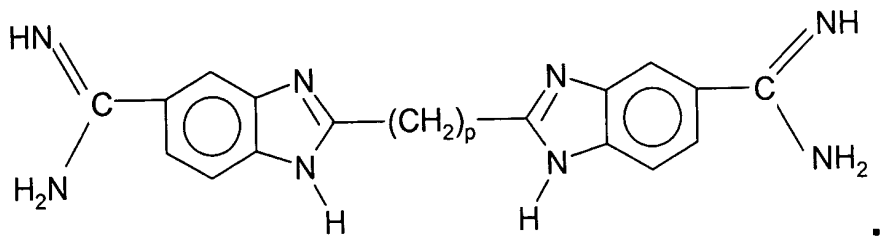


A3

14. (once amended) The method according to Claim 13, wherein said compound is represented by the formula:

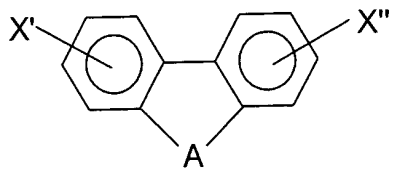


15. (once amended) The method according to Claim 14, wherein said compound is represented by the formula:

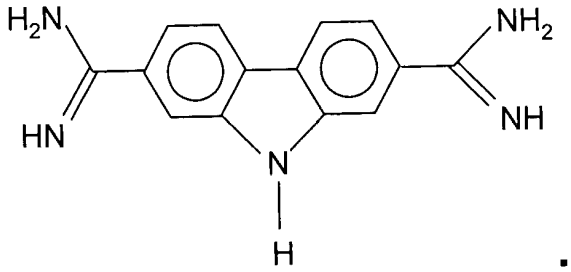


A3 Cont

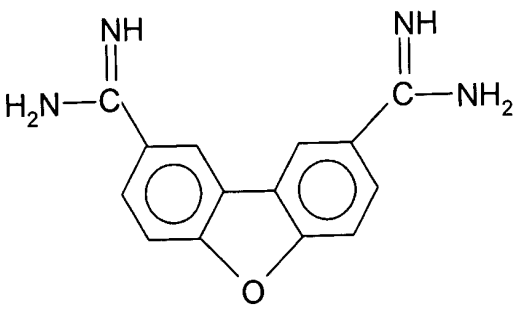
16. (once amended) The method according to Claim 13, wherein said compound is represented by the formula:



17. (once amended) The method according to Claim 16, wherein said compound is represented by the formula:

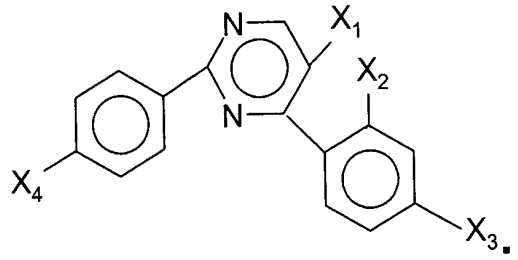


18. (once amended) The method according to Claim 18, wherein said compound is represented by the formula:

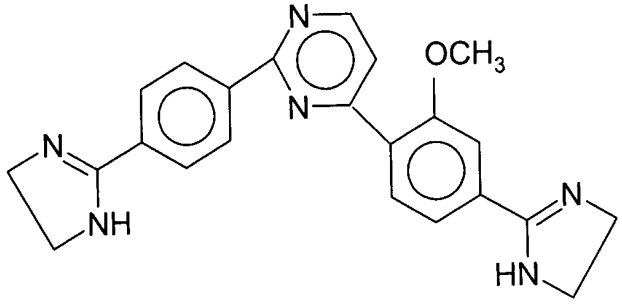


19. (once amended) The method according to Claim 13, wherein said compound is represented by the formula:

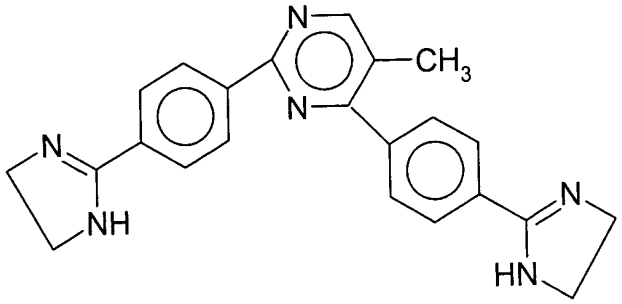
A3 cont



20. (once amended) The method according to Claim 19, wherein said compound is represented by the formula:

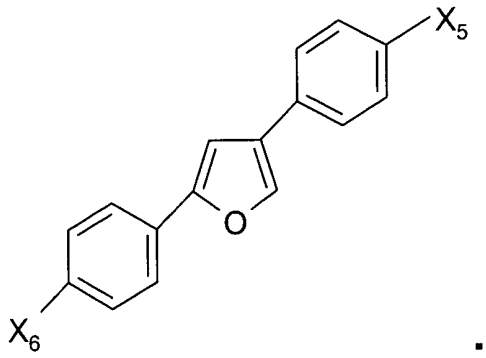


21. (once amended) The method according to Claim 19, wherein said compound is represented by the formula:

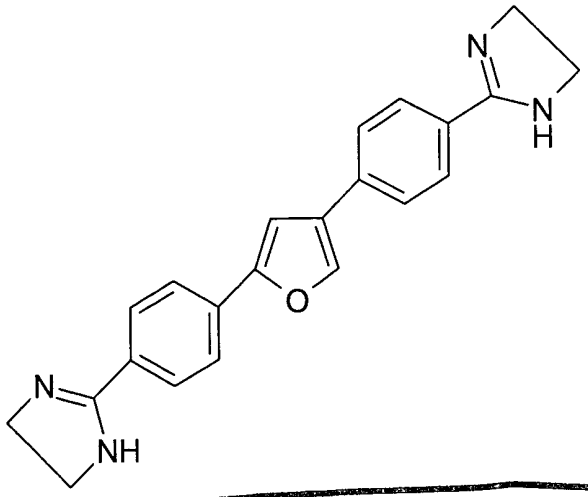


22. (once amended) The method according to Claim 13, wherein said compound is represented by the formula:

A3 cont

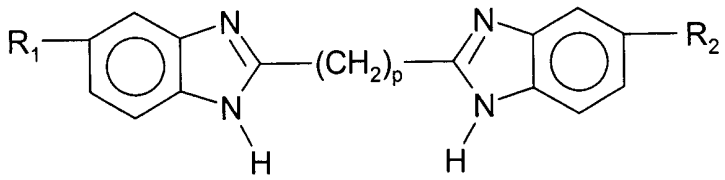


23. (once amended) The method according to Claim 22, wherein said compound is represented by the formula:

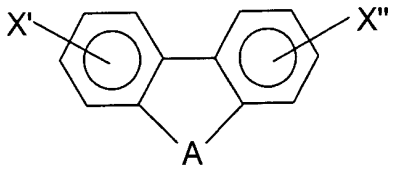


A4

49. (once amended) A pharmaceutical formulation for the treatment of infectious bursal virus disease (IBDV) in an avian subject, comprising a compound selected from the group consisting of:

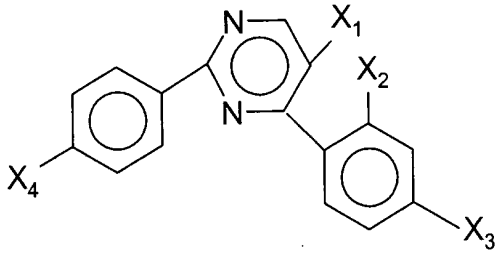


(I)

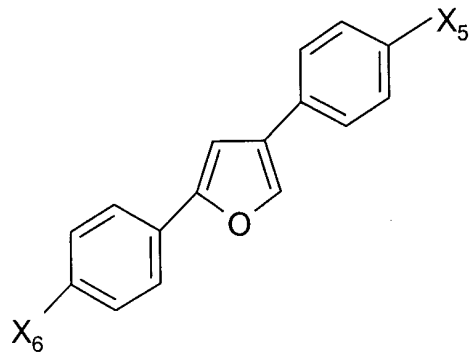


(II)

A 4 cont



(III)



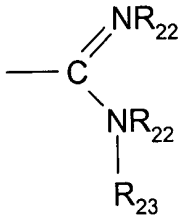
(IV)

or the pharmaceutically acceptable salts thereof, wherein :

p is an integer ranging from 1 to 8;

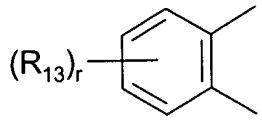
A is selected from O, S, and NR wherein R may be H or loweralkyl;

X', X", X_3, X_4, X_5, X_6, R_1, R_2 are independently selected and each represented by loweralkyl, loweralkoxy, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, alkylaryl, halogen, or:

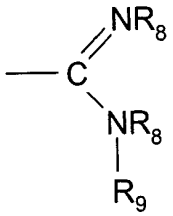


wherein each R_{22} and R_{23} is independently selected from the group consisting of H, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, and alkylaryl, or two R_{22} groups together represent C_2-C_{10} alkyl, hydroxyalkyl, or alkylene; or the two R_{22} groups together represent cycloalkyl or:

AM cont



wherein r is from 1 to 3 and R_{13} is H,



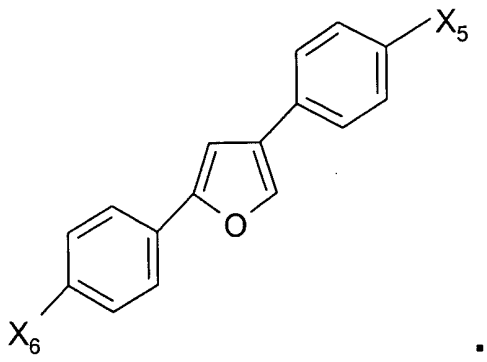
or $-CONHR_{10}NR_{11}R_{12}$, wherein:

R_{10} is loweralkyl; R_{11} and R_{12} are independently selected from the group consisting of H and lower alkyl; each R_8 is independently selected from the group consisting of H, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, and alkylaryl, or two R_8 groups together represent C_2-C_{10} alkylene; R_9 is H, hydroxy, loweralkyl, alkoxyalkyl, hydroxyalkyl, aminoalkyl, alkylaminoalkyl, cycloalkyl, aryl, or alkylaryl; wherein X' and X" may be in the meta or para positions;

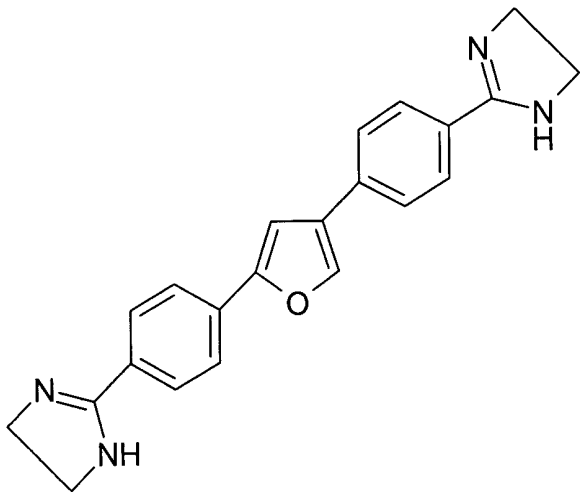
X_1 and X_2 are independently selected from H, loweralkyl, or loweralkoxy; in a pharmaceutically acceptable carrier.

A 5

58. (once amended) The pharmaceutical formulation according to Claim 49, wherein said compound is represented by the formula:



59. (once amended) The pharmaceutical formulation according to Claim 58, wherein said compound is represented by the formula:



REMARKS

I. Status of Claims

Claims 1-59 are pending in the present application. Claim 1-25 have been indicated by the Examiner to be allowed. Claims 26-48 and 50-57 have been withdrawn from consideration, and are cancelled herein without prejudice to the filing of one or more divisional applications thereon. Claims 1, 3-12, 13-23, 49 and 58-59

have been objected to for certain informalities. Claims 49, 58 and 59 stand rejected under 35 U.S.C. §103(a) as being unpatentable over U.S. Patent No. 6,127,554 to Boykin et al. (*hereinafter*, the " '554 patent").

Claims 1, 3-12, 14-23, 49, 58 and 59 have been amended. Support for the amendments to the claims can be found throughout the specification of the present application as filed. No new matter as been added by any of the amended claim language.

Attached hereto is a marked-up version of the changes made to the claims by the current amendment. The attached pages are captioned "Version With Markings To Show Changes Made." Reconsideration of the application as amended and based on the arguments set forth below is respectfully requested.

II. Information Disclosure Statement

The Applicants gratefully acknowledge the Examiner's indication that the Information Disclosure Statements (IDS) received by the Patent Office on July 9, 2002 and February 26, 2002 have been considered. The Examiner has indicated that Reference 14 of the IDS received February 26, 2002 was not considered because of an incomplete copy of the journal article. A complete copy of this reference will be transmitted to the Examiner in the very near future. Upon resubmission of this article, it is respectfully requested that this reference be considered, and its consideration be made of record.

III. Claim Objections

At page 3, item 4 of the Office Action of November 6, 2002, it is stated that "Claims 1, 3-12, 14-23 and 49, 50-59" are objected to for certain informalities. The Applicants respectfully presume that there is a typographical error in this statement, as Claims 50-57 were withdrawn from consideration by the Examiner. The Applicants further presume, in light of statements throughout the remainder of the Office Action, that the Claims that are objected to are Claims "1, 3-12, 14-23 and 49, **58**-59." It is under this assumption that the following statements are made.

Claim 1 has been objected to for certain informalities. Specifically, the Examiner has objected to the term "and" directly before the term "the pharmaceutically acceptable," and has requested that the term "and" be replaced by "or". This substitution has been effected by amendment. The terms "R_3 and R_4" have also been deleted from Claim 1 by amendment at the Examiner's request.

For the purposes of clarification and readability, the term "salt" has been replaced by amendment with the term "salts" in Claim 1 at page 29, line 6. Additionally, the term "and" has been inserted prior to the term "R_2" at Claim 1, page 30, line 1. Finally, the term "is" has been inserted by amendment after the term "R_{23}" at Claim 1, page 30, line 7.

Claim 49 has been objected to for certain informalities. Specifically, the Examiner has objected to the term "and" directly before the term "the pharmaceutically acceptable," and has requested that the term "and" be replaced by "or". This substitution has been effected by amendment. The terms "R_3 and R_4" have also been deleted from Claim 49 by amendment at the Examiner's request.

For the purposes of clarification and readability, the term "and" has been inserted in front of the term "R_2" at Claim 49, page 47, line 7. Finally, the term "is" has been inserted by amendment after the term "R_{23}" at Claim 49, page 48, line 3.

Claims 3-12, 14-23, and 58-59 have been objected to as lacking a period at the end of the claims. A period has been inserted at the end of each of Claims 3-12, 14-23, and 58-59 by amendment.

In light of the foregoing, it is respectfully submitted that satisfaction of formalities for the Claims has been met.

IV. Claim Rejections Under 35 U.S.C. §103(a)

Claims 49, 58 and 59 are rejected under 35 U.S.C. §103(a) as being unpatentably obvious in light of the '554 patent. The Applicants respectfully traverse the rejection for the reasons that follow.

The '554 patent recites certain compounds that are useful in the treatment of *Pneumocystis carinii* pneumonia (PCP). In one embodiment of Formula (I) of the

'554 patent, substituents R_1, R_2, R_3 and R_4 may be hydrogen. When this is the case, then substituents "X" and "Y" correspond to substituents "X_6" and "X_5" of Formula (IV) of the present application.

However, the mere occurrence of one embodiment of Formula (IV) of the present invention in the '554 patent does not render present Claims 49, 58 and 59 obvious. For reasons set forth below, the Applicants respectfully submit that one skilled in the art, with knowledge of the teaching of the '554 patent, would not find it obvious that the compounds described therein would be useful in the treatment of IBDV infection, as claimed in the present application.

Initially, the Applicants note that in order to establish a prima facie case of obviousness, three basic criteria must be met. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference in order to arrive at the present invention. Second, there must be a reasonable expectation of success. Finally, the prior art reference must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must be found in the prior art and not based on the Applicants' disclosure. *See* MPEP § 706.02(j); In re Vaeck, 947 F.2d 488, 20 USPQ 2d 1438 (Fed. Cir. 1991).

Given these criteria for establishing the prima facie case of obviousness, the Applicants respectfully submit that such a prima facie case has not been established. Turning first to the third criteria, the recitation in Claims 49, 58 and 59 of a "formulation for the treatment of IBDV" is a claim limitation that is very clearly not taught or suggested in the prior art reference. Claims 49, 58 and 59 are directed to pharmaceutical formulations for the treatment of infectious bursal disease virus infection in an avian subject. In contrast, the compounds set forth in the '554 patent are indicated to be useful in the treatment of *Pneumocystis carinii* pneumonia (PCP) in mammals. As the Examiner is aware, the infectious agent of IBDV is a virus, while the infectious agent of PCP is not. The '554 patent contains no teaching or implication that its compounds and formulations would have any therapeutic efficacy

against any other disease other than PCP. Thus, there is no suggestion or motivation in the '554 patent that its compounds would be of use in treating IBDV infection. One skilled in the art would not have a reasonable expectation that a formulation useful in the treatment of a PCP infection would also have usefulness in the treatment of a viral disease that infects a different species, and the Patent Office has provided no evidence, experimental or otherwise, to indicate otherwise.

Applicants respectfully note that in reviewing a claim as to its patentability, the claim must be reviewed and examined as a whole, rather than element by element. *Texas Instr., Inc. v. United States ITC*, 6 USPQ2d 1886, 846 F.2d 1369 (Fed. Cir. 1988). The presence of one element of the present invention in the '554 patent (*i.e.*, one embodiment of Formula (IV)) does not render the present claims obvious, when the claims of the present invention are read as a whole.

The Patent Office has stated the "it has been held that a prior art disclosed genus of useful compounds is sufficient to render prima facie obvious a species falling within the genus," citing the cases In re Susi and Merck and Co. v. Biocraft Laboratories. *See* Office Action of November 6, 2002, page 5. Respectfully, the Applicants note that these two cases are entirely distinguishable from the present case at hand, and do not stand for a proposition that renders the present claims unpatentable.

The Susi and Merck cases dealt with cases in which claims directed to novel compounds were at issue. In other words, the applications at issue in Susi and Merck presented claims to new compounds, which were deemed to be particular species of compounds in which a genus encompassing the species had been previously claimed and patented in the prior art. The present application is entirely distinguishable in this regard. Claims 49, 58 and 59 are **not** directed to compounds, *per se*, in which the novelty of all particular embodiments of all the compounds therein are asserted, and which compounds may be claimed in the prior art. Claims 49, 58 and 59 are directed to formulations with a specific use, namely, the treatment of IBDV infection. In that the claims of the '554 patent are directed to entirely different subject matter than the present claims 49, 58 and 59 (*i.e.*, novel compounds

in the '554 patent vs. pharmaceutical formulations with a specific therapeutic use in the present application), it is not possible for the claims of the present application to even be species of a genus set forth in the '554 patent. Accordingly, the holdings of the Susi and Merck cases are not applicable to the present application, and do not stand for any proposition that can render the claims of the present application unpatentable.

With regard to the use of the pharmaceutical formulations of Claims 49, 58 and 59, the Patent Office has stated that "the recitation of the intended use of the claimed invention must result in a structural difference between the claimed invention and the prior art in order to patentably distinguish the claimed invention from the prior art. If the prior art structure is capable of performing the intended use, then it meets the claims." *See* Office Action of November 6, 2002, page 5. In supporting this assertion, the Examiner cited the cases In re Casey, 370 F.2d 576, 152 USPQ 235 (CCPA 1967) and In re Otto, 312 F.2d. 937, 136 USPQ 458 (CCPA 1963). Finally, and in light of these cases, the Patent Office states that "the disclosed pharmaceutical compositions of the compounds embraced by formula I [of the '554 patent] would be capable of treating IBDV." The Applicants respectfully traverse this rejections for the reasons set forth below.

Initially, the Applicants strongly note that the **MPEP itself** has strictly limited the use of these two cases, and the line of cases to which they belong, to "claims directed to machinery which works upon an article or material in its intended use. It does not apply to product claims [.]" *See*, "Material or Article Worked Upon By Apparatus," MPEP § 2115 (Eighth Edition, August 2001), page 2100-57, column 1 (emphasis added). Examining the subject matter of these cases, it is easy to recognize the rationale behind such a clear prohibition on the use of these cases in matters outside the realm of apparatus and machinery.

The Casey case related to an apparatus claim reciting a "taping machine comprising a supporting structure, a brush attached to said supporting structure . . . and means for providing relative motion between said brush and said supporting structure while . . . adhesive tape is adhered to said surface." MPEP § 2115. In the

Otto case, the claims were directed to a core member for hair curlers and a process for making a core member for hair curlers. The court found, in Otto, that the intended use of hair curling was of no significance to the structure and process of making the hair curler core members. MPEP §2111.02. To the extent that the term "structure" is used in these cases, it is limited to the physical structure of machinery and apparatus that are used to act on materials.

Clearly, and on the authority of the Patent Office itself, the Casey and Otto cases carry no weight as regards to the patentability of Claims 49, 58 and 59. None of these claims relates to a machine or apparatus, but on pharmaceutical formulations for the purpose of treating IBDV infection in avians. Moreover, the Patent Office's statement that "the disclosed pharmaceutical compositions of the compounds embraced by formula I [of the '554 patent] would be capable of treating IBDV" is impermissible hindsight. It is well-established law that in deciding obviousness, one must look at prior art from the vantage point in time prior to when the invention was made. In re Carroll, 601 F.2d 1184, 202 USPQ 571 (CCPA 1971). At the time of the invention of the present application, it was not known that the compounds recited therein could be useful for the treatment of IBDV infection, and the Patent Office has provided no evidence to the contrary. This fact is revealed not least because the one reference cited by the Patent Office to support the obviousness rejection, the '554 patent, makes no reference whatsoever to the use of its compounds in the treatment of IBDV infection.

In light of the foregoing arguments, the Applicants respectfully submit that the Patent Office has not met its burden of establishing a prima facie case of obviousness. The sole cited reference in support of this rejection, the '554 patent, provides no suggestion or teaching that the compounds of the present invention might be used in a formulation to treat IBDV infection, nor any reasonable expectation of success. Moreover, the reference does not recite all the limitations of the claimed invention. Accordingly, it is respectfully requested that the outstanding rejection pursuant to 35 U.S.C. §103(a) be withdrawn.